## Multimodal fast optical interrogation of neural circuitry.

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**Authors:** Feng Zhang, Li-Ping Wang, Martin Brauner, Jana F Liewald, Kenneth Kay, Natalie Watzke, Phillip G Wood, Ernst Bamberg, Georg Nagel, Alexander Gottschalk, Karl Deisseroth

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**Public Summary:**

**Scientific Abstract:**
Our understanding of the cellular implementation of systems-level neural processes like action, thought and emotion has been limited by the availability of tools to interrogate specific classes of neural cells within intact, living brain tissue. Here we identify and develop an archaeal light-driven chloride pump (NpHR) from Natronomonas pharaonis for temporally precise optical inhibition of neural activity. NpHR allows either knockout of single action potentials, or sustained blockade of spiking. NpHR is compatible with ChR2, the previous optical excitation technology we have described, in that the two opposing probes operate at similar light powers but with well-separated action spectra. NpHR, like ChR2, functions in mammals without exogenous cofactors, and the two probes can be integrated with calcium imaging in mammalian brain tissue for bidirectional optical modulation and readout of neural activity. Likewise, NpHR and ChR2 can be targeted together to Caenorhabditis elegans muscle and cholinergic motor neurons to control locomotion bidirectionally. NpHR and ChR2 form a complete system for multimodal, high-speed, genetically targeted, all-optical interrogation of living neural circuits.